The evaluation of the incidence of hypoglycemia at induction in children under the age of five undergoing elective surgical procedures - a prospective, single-blinded, observational study.'

This Dissertation is in partial fulfillment of the requirements for the M.D. Degree (Branch X) Anaaesthesiology Examination ot The Tamil Nadu Dr. M.G.R. Medical University, Chennai, to be conducted in April 2013.

C E R T I F I C A T E

This is to certify that the dissertation entitled **The evaluation of the incidence of hypoglycemia at induction in children under the age of five undergoing elective surgical procedures - a prospective, single-blinded, observational study.'** is the bonafide original work of Dr. Cephas Satyanandan, towards the M.D. Branch-X (Anaesthesiology) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai, to be conducted in April 2013.

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CONTENTS :

1. INTRODUCTION :

Preoperative fasting is the practice that requires a patient to be nil per oral (refrain from oral food and liquid intake) for a pre determined period of time prior to a surgical procedure. This is aimed at preventing the regurgitation of stomach contents which in turn can lead to pulmonary aspiration during general anesthesia [1].

It must however be kept in mind that fasting patients for longer than the optimum period can be detrimental to their health [2] especially in children and specifically those in the younger age . However studies as well as common knowledge suggests that overfasting is indeed a frequent practice [3].

This problem of “over fasting” is mainly secondary to the practical difficulties associated with running a theatre list like unforeseen rescheduling and cancellation or addition of procedures which inevitably lead to skewed fasting times.

In this study we have evaluated two hypothesis .

Firstly whether hypoglycemia plays a part in such children who have for various reasons been fasting for longer than required and if routine measurements of blood sugar levels are required prior to surgical

procedures.

Though there have been studies done to assess the association between prolonged fasting and hypoglycaemia these have been on other population groups. Studies on our population group have been few and inconclusive. Hence there was a need to carry out a study with a sufficiently large sample size to establish a causal relationship between the two if any.

The other hypothesis is that the duration of pre operative fasting may be a significant contributor in prolonging the recovery of a child in the early post-operative period. Efforts to support this hypothesis have mostly been based on anecdotal evidence.

We aim to determine if there is a time limit within which these factors play a role, if changes need to be made in routine pre operative practices in our hospital, and if further investigations and/or interventions need to be planned.

2. AIM:

The aim of this study was to evaluate the incidence of hypoglycemia in children under the age of five undergoing elective surgical procedures at the time of induction.

3. OBJECTIVES:

1. To determine the correlation between preoperative fasting duration and fasting plasma glucose levels.
2. To evaluate the correlation between pre operative fasting and post operative awakening time.

4. REVIEW OF LITERATURE

The review of literature is divided into the following topics:

4.1 The fasting order

4.2 The Evolution of the fasting order

4.3 The pre operative fasting order and hypoglycemia at induction

4.4 Effects of prolonged fasting in children

4.5 Delayed awakening in children

4.1 THE FASTING ORDER

Preoperative fasting is the practice that requires a patient to be nil by mouth (refrain from oral food and liquid intake) for a pre determined period of time prior to the induction of anaesthesia.

The primary rationale for preoperative fasting is to prevent the regurgitation of stomach contents into the airway and pulmonary tissue complex while under the effects of general anesthesia. Such regurgitation of as little as 35-45 ml can increase morbidity and even cause death during a surgical procedure. Hence fasting is recommended to reduce the volume of stomach contents by as much as feasible. There are a variety of factors that can predispose to regurgitation of gastric material such as light plane of anesthesia, pregnancy, obesity, difficult airway, emergency surgery (since pre operative fasting duration is often reduced), patients with full stomach and impaired gastric motility. Increased fasting times limits injury if aspiration occurs.

Over and above these fasting orders, it is common for an antacids to be prescribed the previous night (or the

same morning for a procedure scheduled later in the day).

It is usual for these antacids to be repeated again one hour before the induction of anaesthesia. Such administration of antacids exerts its beneficial effect by making the pH of stomach contents more neutral. This helps minimize the damage caused by regurgitation of stomach contents, should it unfortunately happen. H_2 receptor blockers such as ranitidine are also administered for high-risk patients and are usually prescribed in a similar manner to the antacids (with respect to time of administration).

Gastroparesis (impaired gastric emptying) may occur and is frequently caused by metabolic abnormalities such as uncontrolled diabetes mellitus, decreased gastric peristalsis such as seen post trauma and gastric oulet obstruction like in pyloric stenosis). Impaired gastric emptying more frequently impairs the emptying of the stomach contents of foods like vegetables which are rich in cellulose content. Gastric emptying of clear liquids like water or clear juice are only affected when gastric emptying is highly impaired [4].

Therefore, gastroesophageal reflux may be associated with delayed gastric emptying of solids, in situations

where rate of emptying of clear fluids from the stomach has not been affected.

In addition to the above increased intra-abdominal pressure such as seen in obese subjects increase the risk of pulmonary aspiration. Some drugs such as opiates can also markedly slow down emptying of gastric contents. Impaired gastic motility can frequently be detected by certain clinical features like the presence or absence of normal or reduced bowel sounds [5].

Nevertheless it is important that patients present to the operative suite having fasted for an optimum period of time. Not too short so as to avoid the above mentioned complications. Not too long either so as to avoid the many complications of prolonged starvation which are discussed in detail in a later section.

4.2 The Evolution of the fasting order

The minimum fasting times required before the induction of anesthesia have long been a matter of debate. The tradition of preoperative fasting came into vogue in the middle of the 19th century to minimize vomiting associated with the agent prevalent at that time namely chloroform [6]. Literature from that period is full of observations of patients with serious complications associated with induction of anaesthesia on patients who were full stomach , without the necessary precautions. As practitioners of that period became aware of the fact that a recent oral intake especially of solids heightened the risk of chloroform-associated vomiting, the practice of pre operative fasting was gradually introduced into their practice. They however allowed patients to drink clear liquids until a few hours before the procedure. As a matter of fact, the father of antisepsis in the field of surgery , Joseph Lister who had a surgical practice in England during this period of time wrote what probably was the first published preoperative fasting guidelines, clearly differentiating between the effects of solids and liquids on patients anesthetized with chloroform. Around the

1880s , Lister recommended that patients could have clear fluids about 2 hours before surgery [7], but “there should be no solid matter in the stomach”.
He advised practitioners that, "While it is desirable that there should be no solid matter in the stomach when chloroform is administered, it will be found very salutary to give a cup of tea or beef-tea about two hours previously" [6,7].

By the end of the 19th century, Lister's advice was being followed and patients were commonly permitted a cup of "beef tea" (beef bouillon) a few hours before surgery [8]. The practice of differentiating liquids from solids in preoperative instruction prevailed for the next 80 years, textbook fasting guidelines of 2–3 hours for clear liquids and 4–6 hours for easily digestible solids. These were consistent with the known rapid gastric emptying of clear liquids and the slower digestion and emptying of solids. All this gradually changed after World War II, when Mendelson documented an asthma-like syndrome of expiratory wheezing, dyspnea, cyanosis, and pulmonary lesions following the aspiration of stomach contents by obstetric and laboring patients who were under general anesthesia and not intubated [7, 9,10,11]. Soon after, the standard of care for surgical patients changed from the aforementioned practice to one that was to prescribe

NPO after midnight [7,10,11,12]. to all patients irrespective of the planned patient schedule .

The first proposition from a society came from British anesthetists stating that patients should be nil by mouth from midnight [13]. By the 1960s most American anesthesia textbooks too had changed, without new evidence, to NPO after midnight.

Around this time a set of studies in Calgary, Canada demonstrated wide inter-patient variability in gastric fluid volume at induction of anesthesia in healthy patients. Mean volume was less in those who drank 150 mL water 2–3 hours preoperatively than in those who received NPO from midnight, most of whom had had no oral intake for 12–18 hours. In 1990 guidelines of the Canadian Anaesthetist's Society, suggested a total fast of no less than 5 hours [14] .

Soon thereafter, the American Society of Anesthesiologists (ASA), followed by the Association of Anaesthestists of Great Britain and Ireland (AAGBI), recommended new fasting guidelines for the minimum fast prior to surgery [15]. These guidelines were similar to the ones laid down by the Canadian Anaesthetists society. This was based upon new evidence in studies done elsewhere which yielded similar evidence . Namely that drinking clear fluids two hours prior to surgery

decreased pulmonary aspiration compared to those nil by mouth since midnight.

Further studies from Calgary and other centres, were done with subjects drinking 150–450 mL or more of clear liquid (water, black coffee or tea, fruit juice) until 2–3 hours before surgery. Overall if was found that such intake of fluids did not increase gastric fluid volume compared with NPO from midnight. The salient conclusions from these studies was that if volume was not increased, the risk of pulmonary aspiration was not increased.

Subsequently there were various guidelines from the different societies. Though these were guidelines issued by independent bodies they followed the principles discovered in the preceding studies. Hence all the various guidelines bore more similarities to each other than differences. In 1999, the American Society of Anesthesiologists published preoperative fasting guidelines of 6 hours for easily digested solids and 2 hours for clear liquid for healthy patients scheduled to undergo elective surgery [15].

The Canadian Anesthesiologists' Society adopted similar guidelines the following year [16] .

These have found widespread usage and have since become standard practice the world over and is what is practiced in our institution as well .

The following are the currently recommended guidelines for nil by mouth prior to surgery :

AMERICAN SOCIETY OF ANAESTHESIOLOGISTS FASTING GUIDELINES	
INGESTED MATERIAL	MINIMUM FASTING (IN HOURS)
Clear liquids	2
Breast milk	4
Infant formula	6
Non human milk	6
Light meals	6
Fasting times apply to all ages Examples : water, fruit juice without pulp, carbonated beverages, clear tea black coffee. Examples : dry toast and clear liquid. Fried or fatty foods may prolong gastric emptying time. Both amount and type must be considered. The guidelines do not recommend the routine use of gastrointestinal stimulants, gastric acid secretion blockers or oral antacids.	

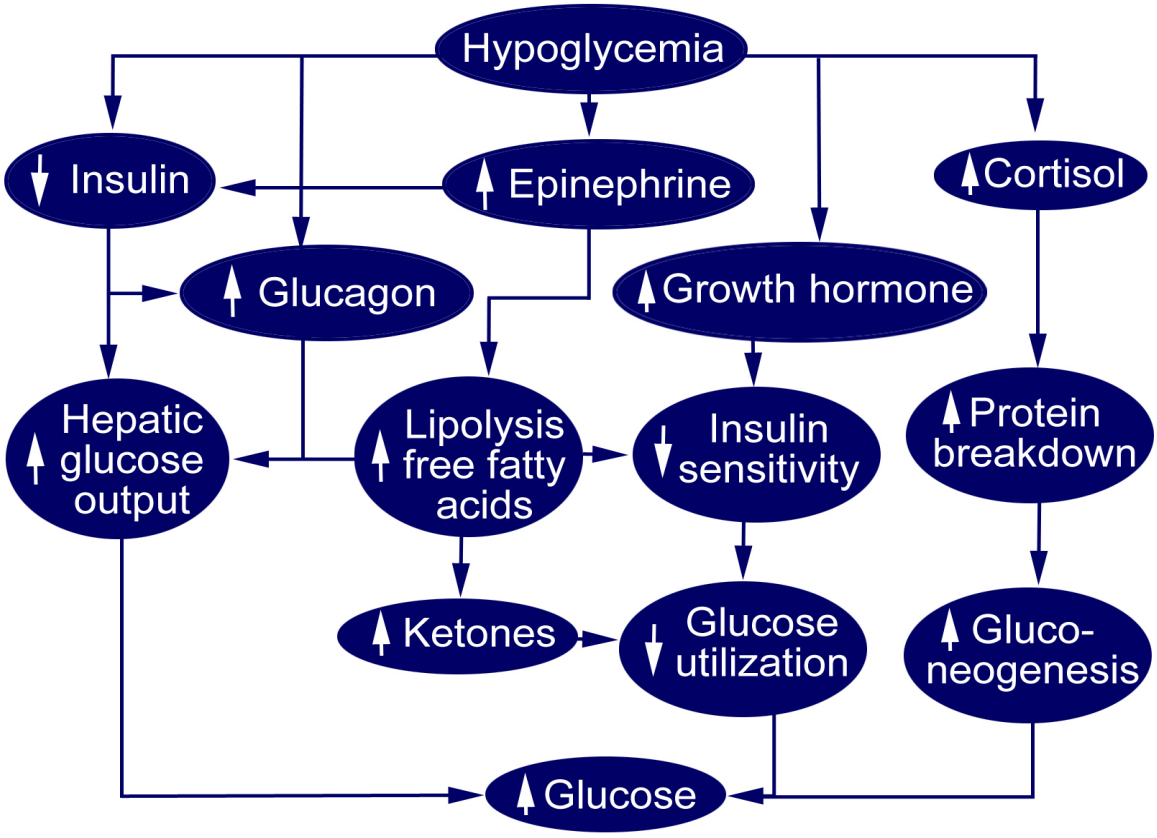
4.3 THE PRE OPERATIVE FASTING ORDER AND HYPOGLYCEMIA AT INDUCTION

Hypoglycemia in children predisposes to lethargy, irritability, metabolic acidosis and other complications including seizures [17].

Infants and children with asymptomatic hypoglycemia have been shown to have neurocognitive defects at the time of hypoglycemia. These include impaired auditory and sensory-evoked responses and impaired test performance.

The long-term consequences of hypoglycemia include decreased head size and lowered IQ. Radiological studies have also revealed specific regional brain abnormalities observed using magnetic resonance imaging (MRI).

Under normal circumstances hypoglycemia is prevented by a tightly controlled regulatory mechanism.



GLUCOSE HOMEOSTASIS

The above figure draws light on the various homeostatic factors that usually keep glucose levels within the normal range.

This delicate balance may be rendered ineffective in the presence of metabolic disorders or abnormal circumstances like prolonged starvation, periods of acute stress among others.

Despite clear-cut fasting guidelines[18] and sincere efforts of anaesthesiologists to implement them, uncertainties in case schedules, unforeseen cancellation of cases,

subsequent adherence to overnight fasting policy and failure to comply with preoperative fasting instructions often lead to prolonged preoperative fasting. This could be because of the fact that the fasting guidelines have been drawn up mainly with an aim to minimize the risk of aspiration[18]. The association between preoperative fasting and hypoglycemia has been controversial. Various studies done at different points in time have shown levels of hypoglycaemia ranging from 10% to 30%[19-25]. as well as studies showing no effect on blood glucose levels after prolonged periods of fasting.[26] There is only one published study from India which showed significant levels hypoglycaemia at induction[27]. This study was done with a relatively smaller sample size and on a cohort of much older children. Hence there was a need for a study with a larger sample size to look at the same in an Indian population.

The objective of this study was to find the correlation between preoperative fasting duration and fasting plasma glucose levels, and to determine if pre operative measurement of blood glucose is indicated in patients with prolonged periods of fasting

The study also looked at the correlation between pre operative fasting and post op awakening time. Hypoglycaemia is known to cause delayed awakening in children. We sought to establish an association if any, between pre operative fasting and delayed awakening.

4.4 EFFECTS OF PROLONGED FASTING :

Despite the presence of clear guidelines with regards to pre operative fasting it is apparent that a large number of children do end up fasting for periods much longer than those established in the guidelines. These can to attributed to some commonly held notions such as :

Overnight fasting from all manner of food intake is the safest method to reduce the risk of pulmonary aspiration during anesthesia.

Clear liquids ingested up to two hours before surgery increase the risk of vomiting and pulmonary aspiration.

The belief that gastric emptying time is the same for clear fluids as well as full liquids (those that are not transparent, such as milk, creamed soup, and some varieties of fruit juice) and solids.

These age old notions which may have held true with the medical practices and protocols of that era do not really apply in modern medicine. In fact, increased awareness of risk factors for aspiration, together with modern anesthetic practices [28,29,30,31,32,33,34] and improved anesthetic agents, has dramatically reduced the risk of pulmonary aspiration.

As for stomach contents at the time of surgery, rates of gastric emptying vary widely, depending on the type of liquid or food consumed [28,29,30]. Clear liquids leave the stomach almost immediately, while full liquids and solids remain for significantly longer periods. It has long been established that patients who drink clear liquids a few hours before surgery have significantly lower gastric volumes and similar or higher pH values compared with those who fast overnight, suggesting that drinking clear liquids may stimulate gastric emptying and dilute acidic gastric secretions, thereby lowering the risk of pulmonary aspiration and increasing patient safety [31,32,33,34,35,36]. Large studies show a progressive decline in aspiration incidence, from 0.15% in 1946 [37] to 0.006% in 2002 [38]. Hence it is apparent that based on current evidence that erring on the side of caution by recommending overzealously long fasting orders may in fast increase the risk of the same.

In addition to the above other byproducts of such prolonged fasting such as thirst, hunger, anxiety, drowsiness, and dizziness, excessive preoperative fasting may have adverse physiologic effects, including dehydration, insulin resistance, postoperative hyperglycemia, muscle wasting, and a weakened immune response [34,35,36]. Clear liquids, on their own , may not be enough to keep such side effects at bay .

Recent evidence shows that, over and above clear fluids upto two hours before procedures , the optimum method to prevent the unwanted side effects of preoperative fasting is to order for a carbohydrate heavy clear drink to be had two to three hours before induction of anaesthesia or prior to sedation [30, 34, 35, 36, 37]. This method of preoperative preparation has been shown to decrease insulin resistance in the post operative period [38-47] as well as nausea ,vomiting [46] and loss of muscle strength during the same time frame [40] . This has also been been shown to reduce the duration of hospital stay [46]. With the emergence of such strong evidence in favour of pre operative carbhohydrate loading over the past ten years a large number of socities and associations of physicians like the European Society for Clinical Nutrition and Metabolism [30], the British Association for Parenteral and Enteral Nutrition, the Association for Clinical Biochemistry, the Association of Surgeons of Great Britain and Ireland, the Society of Academic and Research Surgery, the Renal Association, the Intensive Care Society, and the Scandinavian Society of Anaesthesiology and Intensive Care Medicine have all endorsed guidelines that recommend providing a carbohydrate-rich clear beverage two to three hours before surgery, in addition to other clear liquids.

4.5 DELAYED AWAKENING IN CHILDREN :

Causes of delayed awakening in children are many but the below are the most frequently cited causes [48] .

These can be divided into the following :

4.5.1 Prolonged drug action

4.5.2 Respiratory causes

4.5.3 Metabolic causes

4.5.4 Neurological causes

4.5.1 Prolonged drug action :

Delayed awakening can be caused due to residual effects of drugs after surgery most commonly due to the following

- **Overdose.**

  This can occur if the child has been given much more than the recommended dose or the child is more sensitive to the drug. This can also be seen in cases where there is a slowdown of metabolism of the drugs like in hepatic or renal failure. In such cases smaller doses may be required. In certain conditions there may be increased sensitivity to particular agents.

For example in myasthenia gravis there is greatly increased sensitivity to non-depolarising muscle relaxants.

- **Duration and type of anaesthetic given.**

The time taken for awakening when inhalational anesthetic agents are used is directly proportional to alveolar ventilation. Therefore, inadequate ventilation is a common cause of delayed awakening. Awakening duration is also inversely related to the inhalational agents's blood gas solubility, so relatively insoluble agents like desflurane and nitrous oxide are washed out much quicker than more soluble ones like halothane. For long duration surgical procedures, time to awakening is also affected by the total amount of drug taken up by the tissues which in turn depends on the solubility of the drug in various tissues, amount of anaesthetic used and duration of time for which the patient was under anaesthesia.

For intravenous induction agents like propofol and thiopentone, recovery from induction is dependant to a large extent on the redistribution of the drug from the brain and blood to fat and muscle.

Propofol, since it is rapidly metabolised by the liver and at other extrahepatic sites as is widely believed, patients who are induced with propofol as well as those for whom it has been used for maintenance recover much faster than those who have been given other agents. Elimination half life for this drug is relatively fast (10 to 70 minutes). Due to these factors it does not accumulate in the body.

With respect to thiopentone, while the initial drug effect is terminated within 4 to 20 minutes by redistribution, elimination happens by oxidative metabolism in the liver. This happens at a rate of about 12% - 15% every hour. As a consequence, Thiopentone has a prolonged elimination half life lasting from 3.5 upto 22 hours and as high as 1/3rd of the drug may remain in the tissues even after 24 hours. As a result , cumulative effects can be seen in patients when more than a single dose of the drug is administered. For most of other commonly used intravenous anesthetic drugs, the termination of drug action depends on the time required to metabolise or excrete the drug. Other factors like advanced patient age, renal or hepatic dysfunction can prolong the duration of action of these drugs.

- **Potentiation by other drugs**.

  Drugs such as diazepam with are routinely used for premedication as well as other drugs including alcohol are also known to contribute to delayed awakening. They do so by potentiatiating the central nervous system depressant effects of anaesthetic and analgesic drugs.

- **Prolonged neuromuscular blockade.**

  Residual neuromuscular blockade post procedure can lead to muscle weakness. This can paint a picture which is frequently confused with delayed awakening though the patient may be fully conscious and aware. This could be due to overdose or incomplete reversal of non-depolarising muscle relaxants or in a patient with Scoline apnoea. In such a setting a nerve stimulator can aid in the diagnosis. The ability to maintain a head life for 5 seconds is indicative of adequate reversal. Conversely inability to do the same indicates residual blockade at least 25% of the receptors.

The typical twitchy movements of partial reversal may also be seen, and as a consequence the patient may become distressed and agitated. Prolonged apnoea following suxamethonium "scoline apnoea" is due to an abnormal or absent plasma cholinesterase enzyme. Repeated doses of suxamethonium (>6-8mg/kg total dose) may produce a "dual block" which is prolonged and slow to recover. The newer muscle relaxant mivacurium is also metabolised by plasma cholinesterase and 'mivacurium apnoea' may occur rarely. Patients with myasthenia gravis are very sensitive to non-depolarising muscle relaxants, doses of only 10 to 50% of the usual dose are required and long acting agents like pancuronium should be avoided. In the muscular dystrophies there is also increased sensitivity to muscle relaxants and to all respiratory depressant drugs. In renal failure there is reduced elimination of non depolarizing muscle relaxants such as pancuronium and vecuronium. Large doses of aminoglycoside antibiotics (gentamicin etc) can prolong muscle relaxant action. Acidosis can also have this effect.

4.5.2 Respiratory Causes :

Patients who do not breathe effectively or are apneic during or after anaesthesia may become hypercarbic (elevated PaCo2) to a degree that could produce sedation or even unconsciousness. Risk factors for such include patients with underlying respiratory disease, especially those who exhibit CO2 retention prior to the procedure, high dose opioids, airway obstruction and inadequate reversal from the effect of muscle relaxants. The diagnosis is usually suspected clinically and can be confirmed by an arterial blood gas analysis. Measurement of the end tidal CO2 though not as sensitive and specific are also useful adjuncts. It is to be kept in mind that patients receiving oxygen may have normal SpO2 readings even when levels of CO2 are significantly .

4.5.3 Metabolic Causes :

An underlying metabolic disorder may be responsible for delayed recovery after anaesthesia. The most common conditions include:

- **Hypoglycemia**. This can be seen in small children and those who have been administered OHA's (oral hypoglycaemic agents) or insulin. It may also be seen in patients with liver failure as well as in conditions like septicaemia and malaria which are known to affect the liver.
- **Severe hyperglycemia.** This can also lead to delayed awakening. This can occur in uncontrolled diabetis especially those with hyperosmolar non ketotic diabetic coma as well as diabetic ketoacidosis.
- **Electrolyte imbalance.** This may be as a consequence of the surgical procedure or secondary to other underlying illnesses .
- **Hypothermia**. Severe hypothermia may lead to reduced levels of consciousness. A core body temperature of less than 32^{o}C has a significant anaesthetic effect on its own. It can also potentiate

the CNS depressant effects of other sedatives and anaesthetic agents. In addition to the above hypothermia decreases the MAC value of inhalational agents. This as well as the antagonism of muscle relaxant reversal and slowdown of drug metabolism seen at these body temperatures can lead to delayed awakening.

- **Central anticholinergic syndrome** can occur on rare occasions following the usage of anticholinergic drugs. Drugs like hyoscine are particularly associated with the same but other agents like antihistamines, phenothiazines , antidepressants and pethidine are also known to produce this syndrome. It has also been reported after volatile anaesthetic agents, ketamine and benzodiazepines. It is postulated to be due to a slowdown in the inhibitory anticholinergic activity in the brain and it frequently manifests as confusion, hallucinations, convulsions, restlessness and coma and therefore as delayed awakening from anaesthesia. Peripheral anti-cholinergic effects such as dry mouth, tachycardia, blurred vision may also be seen in these cases. The treatment of choice is with physostigmine 0.04mg/kg given slow iv. The onset of action is within 5 minutes, but features may return after 1-2 hours.

4.5.4 Neurological Causes :

There are two common neurological causes of delayed awakening :

- **Cerebral hypoxia** of any cause will result in reduced conscious level which may first present as delayed awakening from anaesthesia, especially if the hypoxic insult has occurred during anaesthesia.
- **Intracerebral event** such as haemorrhage, embolism or thrombosis. These are very rare except in neurosurgery, cardiac surgery, cerebrovascular and carotid surgery.

At the end of anaesthesia and surgery the patient should be awake and easily arousable, responding to the outside environment , able to protect their airway, maintain adequate ventilation without any assistance and with their pain under control. Time to emerge from anaesthesia is variable and depends on many factors related to the patient, the type of anaesthetic given and the length of surgery.

5. METHODOLOGY:

INITIATION OF THE STUDY :

After approval of the topic and design from the department a small pilot study was conducted on 5 patients. Subsequent to the pilot study protocols were refined after which the proposal was submitted to the institutional review board and ethics committee. Proposals regarding the study were also submitted to the department of pediatric surgery and the department of clinical biochemistry . After due approval and funding was secured from all of the aforementioned , the study was initiated in our department.

STUDY PROTOCOL :

This prospective study was conducted on children (age between 1 to 60 months ; ASA grade 1 and 2) undergoing elective surgery. Written informed consent was obtained from the parent or the guardian. Patients with known metabolic disorders were excluded from the study.

Preoperative fasting instructions was issued in accordance with the recommended guidelines. Premedication was given as deemed necessary by the treating doctors. On the day of the surgery, fasting duration was recorded, that is the time interval between the last feed and time at induction in the operating room. The duration of fasting (excluding water) was noted by looking at records as well as interview of the parents. All procedures in children that require induction of anaesthesia also require establishment of intra venous access either prior to or soon after induction of anaesthesia. A sample of venous blood was taken while obtaining intravenous access after induction of anaesthesia or prior to induction of anesthesia in a co operative child and sent for measurement of plasma glucose levels. A value less than 40mg/dl was taken as hypoglycaemia. Neonates were not included in the study.

After anesthetic induction with incremental doses of Sevoflurane (2 to 4 MAC) , end-tidal isoflurane was maintained at 1.5 MAC (minimum alveolar anesthetic concentration) for 10 minutes . The hemodynamic parameters were recorded at induction and the first half an hour thereafter.

Anesthesia was induced with increasing concentrations of Sevoflurane in oxygen and air (fraction of inspired oxygen, 0.50) via mask and a semiclosed circle system. The inspired Sevoflurane concentrations were within 4 MAC .Soon after consciousness was lost, a peripheral IV catheter will be inserted, and Fentanyl (1.5 ug/kg) was administered along with Atracurium (0.5mg/kg) if required. Immediately following induction the patient was switched over to isoflurane for maintenance of anaesthesia. During normocapnic (end-tidal PCO_2, 35–40 mm Hg) manual ventilation by mask, end-tidal Isoflurane was maintained at 1.5 times the age-specific MAC for 10 minutes to allow myocardial uptake of isoflurane (at least 4 times the myocardial time constant for isoflurane). Thereafter levels of isoflurane were adjusted based on the hemodynamic response. The time at induction as well as the time at intubation were noted. Additional doses of Fentanyl were also given to attenuate hemodynamic response. Changes in isoflurane were recorded.

Peak inspiratory pressure during manual ventilation was maintained within a range of 14–18 cm H_2O. The position of the patient and timing of noxious stimuli, such as tracheal intubation or surgical incision, during the study period were noted. All other modalities used to treat pain were noted – Caudal, Epidural, opoids , NSAIDS.

Body temperature was maintained by the use of warming blankets and/or radiant heating lamps. IV fluids were administered based on the routinely followed protocols. Inspired and end-tidal carbon dioxide were monitored with an infrared respiratory gas monitor. Respiratory gases were sampled from the inlet of low-dead-space closed breathing circuits. Heart rate (HR) and systolic arterial pressure (SAP) and mean arterial pressure (MAP) were monitored noninvasively by using an automated blood pressure device .These were recorded at 5 minute intervals.

At the end of the procedure the time at which the inhalational agents were cut off was noted. The time at eye opening was also noted either by the treating anaesthesiologist or the staff in the post operative suite under whose care the recovery was being monitored.

Duration of time to eye opening was calculated as duration of time from discontinuation of inhalational agent to opening of eyes either spontaneously or on verbal prompting repeated every minute.

The blood for the glucose study were collected in tubes containing Fluoride preservatives.

VACUTAINER TUBE USED FOR SAMPLE TRANSPORT

Sodium fluoride tubes were used for glucose determination. The tubes are available in plastic and can be identified by a grey cap. These maintain plasma glucose at a constant level till the test is performed by inhibiting glycolysis. Fluoride acts primarily by inhibiting enolase in the glycolytic pathway.

Fluoride strongly inhibits the enzyme in the presence of inorganic phosphate. The inhibitory species is the fluorophosphate ion, which when bound to magnesium forms a complex with enolase and inactivates the enzyme.

These were then sent through a chute system to the biochemistry lab where the blood sugar levels analysis were performed in modular systems which use the glucose oxidase peroxidase method for the same after the tubes have been centrifuged at around 1300g for 10 minutes at room temperature.

This P800 system is manufactured by Hitachi company Japan and marketed by Roche, Germany . The reagents were also supplied by Rosche diagnostics along with calibrators provided by the company. The results were validated by performing several quality control samples manufactered by Biorad, Rosche and internal quality control samples.

HITACHI P800 MODULAR SYSTEM

These reports were collected at periodic intervals and entered into the relevant data sheets.

Data analysis as well as regression analysis to elucidate correlations between the many variables were performed. All data analysis was done using the software SPSS 14.0 and Microsoft Office Excel 2007.

KEY INCLUSION / EXCLUSION CRITERIA :

Inclusion Criteria:

1. Paediatric surgery patients coming for elective procedures.
2. Age between 1 to 60 months.
3. ASA grade 1 & 2.

Exclusion Criteria:

1. Children with known Metabolic syndromes.
2. Refusal of consent.
3. Emergency surgical procedures.

SETTING OF THE STUDY :

The study was carried out under the Department of Anaesthesiology, Christian Medical College, Vellore in the Centenary building Operating Theatre complex. The subjects were taken from among patients coming for elective surgery under the Department of Paediatric Surgery.

STUDY DESIGN :

The study was designed to be a prospective, single blinded observational study.

BLINDING AND MASKING :

Since this was an observational study we were unable to perform a double blinding. Any other study design would have not passed the scrutiny of the ethics committee of the institution.

OUTCOMES :

Primary Outcome:

Blood sugar levels as measured at the time of induction of anaesthesia .

Secondary Outcomes:

Delayed awakening due to hypoglycemia at the end of the operative procedure.

TARGET SAMPLE SIZE AND RATIONALE :

With an incidence of hypoglycemia being taken as 3.6% based on similar studies performed in the south east Asian population and with an absolute precision of 'δ' (range of values provided below in the table), the sample sizes at 5% level of significance (α) are presented below.

Absolute precision (δ)	**Sample size (n)**
2%	333
1.5%	593
1%	1333
0.5%	5333

The sample sizes were arrived at using the following formula:

$$n = \frac{Z_{1-\alpha/2}{}^2 \times p \times q}{\delta^2}$$

Age was categorized into four groups. Patients were divided into four age groups: less than 10 months, 11–20 months, 21-40 months and 41 -60 months.

Consecutive cases were sampled in blocks of 20 to maintain equal numbers in each age group category. Sample size of 500 was studied for a precision value of close to 1.5%.

STATISTICAL ANALYSIS :

Patients were grouped by duration of preoperative fast (0–4 h, 4–8 h, 8–12 h, and >12 h). The incidence of hypoglycemia were presented along with its respective confidence interval. The relationship between the fasting time before surgery, age and weight, and the plasma glucose levels were assessed using a multiple regression model after assessing their relationship at the univariate level with t-tests and chi-square tests. Receiver operating characteristic (ROC) curve were used to determine the optimal cut-point for fasting time to be screened for potential hypoglycemia. Means and standard deviations were then used to describe demographic data and secondary outcomes. Within each age group, the HR, SAP, and MAP data (baseline values, 1.5 MAC values, and absolute changes from baseline to 1.5 MAC values) were also compared among fasting groups by using one-way analysis of variance, followed *post hoc* by Fisher's protected least significant difference test for multiple means comparisons.

Logistic regression analysis were then used to correlate the duration of fasting with the change in SAP, MAP and HR within each age group. $P < 0.05$ were considered to be statistically significant.

Logistic regression analysis was done to assess the correlation between duration of fasting for liquids and solids. Similar methods were also used to correlate other variable data.

6. RESULTS

TABLE 1 : SEX DISTRIBUTION :

	FREQUENCY	PERCENT
MALE	362	76.2
FEMALE	113	23.8
Total	475	100.0

475 children below the age of 60 months were included in the study of which 362 were males and 113 females.The preponderance of males in the study can be attributed to the fact that a large proportion of surgeries performed at our hospital were urology procedures.

TABLE 2 : AGE DISTRIBUTION :

AGE IN MONTHS	FREQUENCY	PERCENT	CUMULATIVE PERCENT
0-10	114	24.0	24.0
11-20	117	24.6	48.6
21-30	77	16.2	64.8
31-40	63	13.3	78.1
41-50	50	10.5	88.6
51-60	54	11.4	100.0
Total	475	100.0	

At the end of the study the children were approximately equally distributed into the following age group categories - less than 10 months, 11–20 months, 21-40 months and 41 -60 months.

The highest number of children were in the below 20 months category. This reflects the natural distribution of patients coming in for surgery to our paediatric theatres. The reason for restricting this study to children under the age of 5 was because previous studies done elsewhere in other racial groups seem to suggest that this younger cohort of patients is more likely to experience hypoglycaemia after prolonged fasting.

TABLE 3 : WEIGHT DISTRIBUTION :

WEIGHT RANGE	FREQUENCY	PERCENT	CUMULATIVE PERCENT
0-5	30	6.3	6.3
6-10	217	45.7	52.0
11-15	173	36.4	88.4
16-20	53	11.2	99.6
21-25	2	.4	100.0
Total	475	100.0	

As children with metabolic abnormalities were excluded from the study 96.6 % of the children fell within the normal weight range for the age group. The majority of children weighed between 6 to 15 kgs.

GRAPHICAL REPRESENTATION OF WEIGHT DISTRIBUTION :

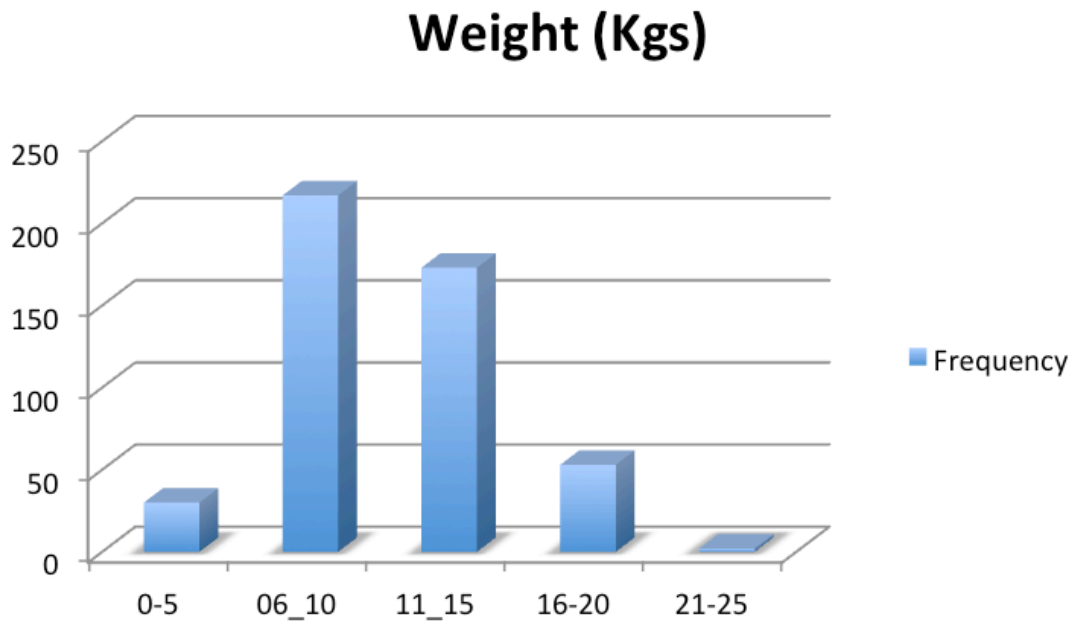


FIGURE 1:

The above chart depicts a graphical representation of the the weight distribution of the subjects.

There were only two patients who fell outside the normal weight for age range. The formula for weight for age used was as follows :

WEIGHT = 2 X (AGE) + 8.

This was done as metabolic disorders as well as extremes of weight are known to alter the normal biochemical processes in the body. Deranged plasma glucose levels can therefore be got in such patients independent off fasting duration.

GRAPHICAL REPRESENTATION OF MEAN WEIGHT AGAINST AGE:

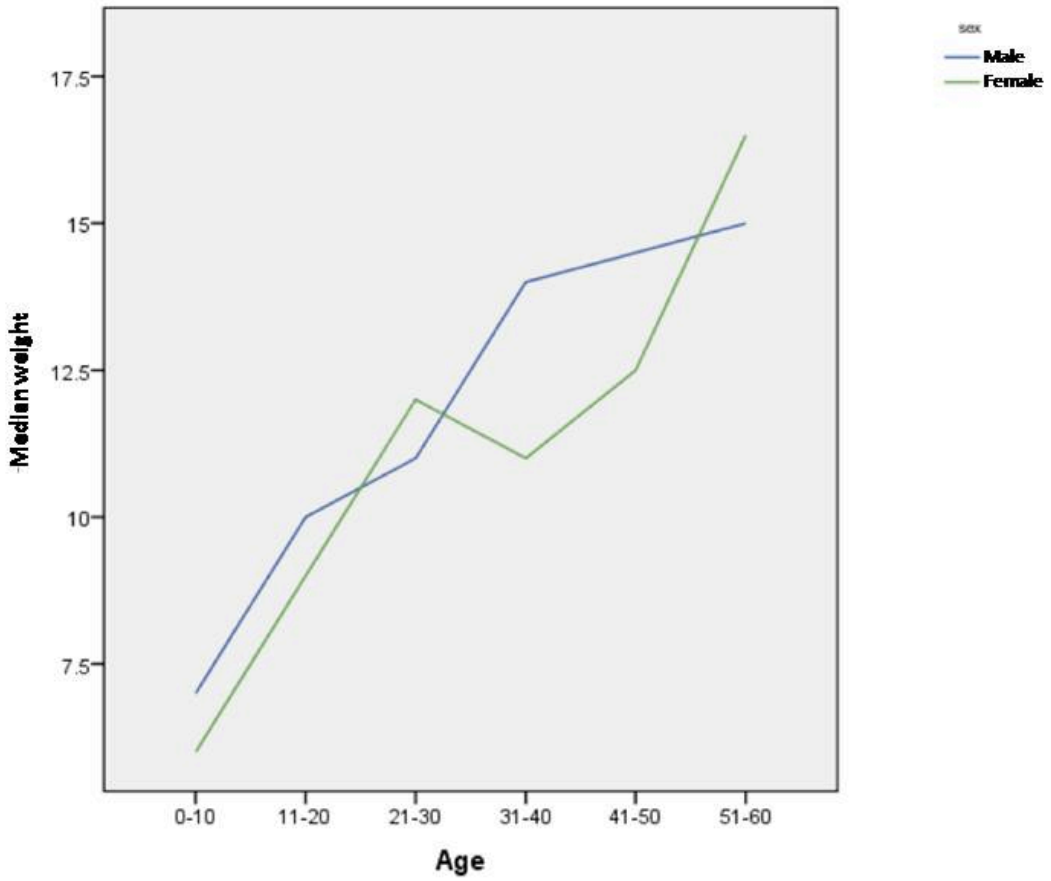


FIGURE 2 :

The above graph shows us the mean weight for different age (in months) categories separated based on gender.

The line in blue represents the males while the line in green represents the female subjects. This graph suggests that the mean weight by age was very similar for both the sexes. This is due to the fact that before the onset of the growth spurt both the sexes follow a very similar growth tragectory.

GRAPHICAL REPRESENTATION OF MEAN WEIGHT AGAINST AGE:

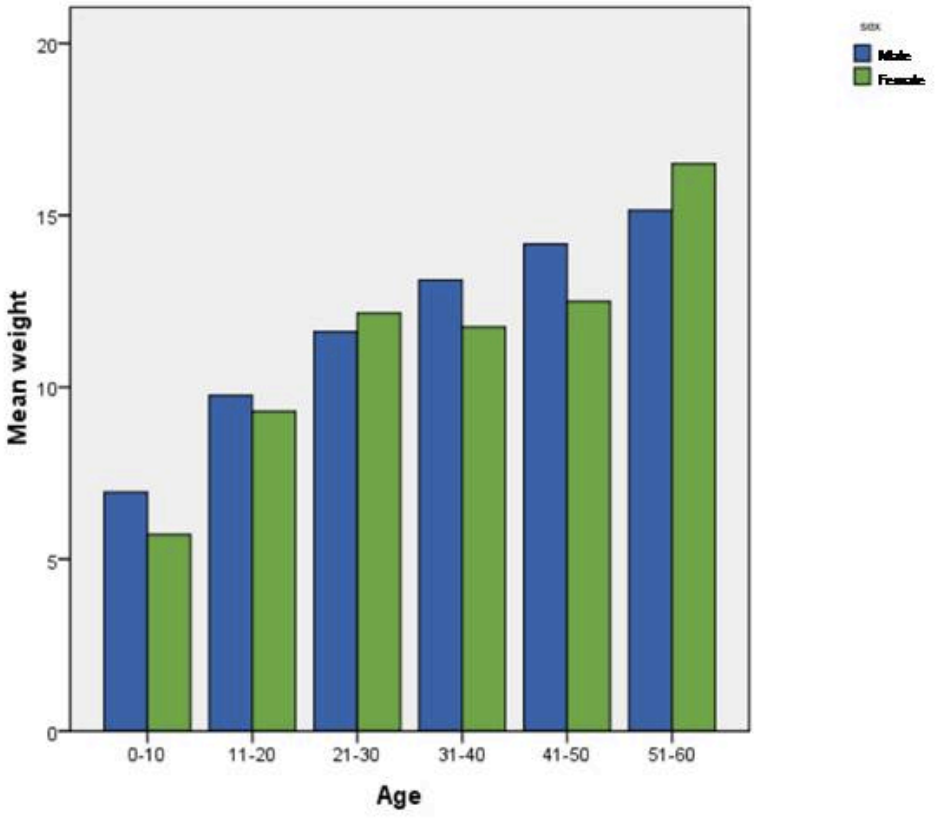


FIGURE 3 :

The above chart represents a graphical depiction of the mean weight of the children separated into age groups with each age group further divided based on sex.

TABLE 4 : CLINICAL FEATURES OF HYPOGLYCEMIA :

HYPOGLYCEMIA	FREQUENCY	PERCENT
YES	4	.8
NO	471	99.2
Total	475	100.0

There were 4 children in the study with clinical features of hypoglycemia . However they all had normal blood glucose levels.

This can be attributed to the fact that the features of hypoglycaemia like irritability, lethargy among others are not very specific. The questionnaire given to the health care providers prior to the case did not mention specific features of hypoglycaemia to look for. Hence the low number of patients with clinical features of hypoglycaemia could be attributed to this lack of standardization.

DURATION OF PREOPERATIVE FASTING :

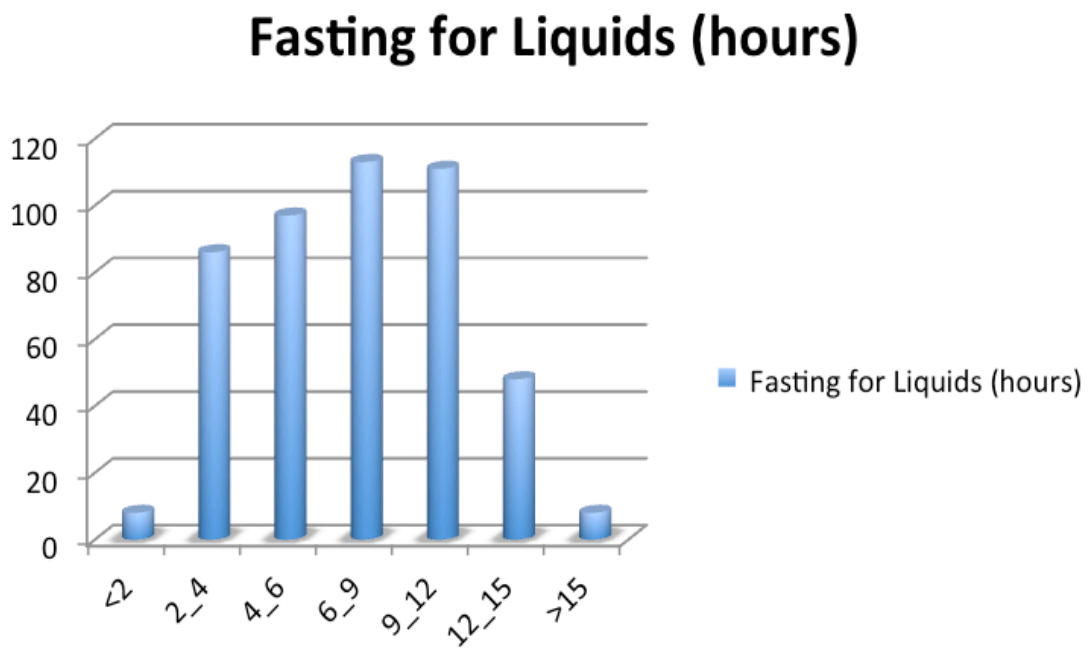


FIGURE 4:

The above graphical representation of duration of fasting with respect to liquids shows that the majority of children had fasted between 6 to 12 hours for liquids.

17 children had fasted for more than 15 hours and 77 children had fasted for between 12 hours to 15 hours.

TABLE 5 : PRE OPERATIVE BLOOD SUGAR LEVELS:

FASTING BLOOD SUGAR	FREQUENCY	PERCENT	CUMULATIVE PERCENT
40-49	9	1.9	1.9
50-59	11	2.3	4.2
60-69	30	6.3	10.5
70-79	77	16.2	26.7
80-89	158	33.3	60.0
90-99	119	25.1	85.1
100-120	61	12.8	97.9
>121	10	2.1	100.0
Total	475	100.0	

There were no children with blood glucose levels below 40 mg/dl.

The lowest blood sugar levels were in the range of 40 – 49 mg/dl. These were observed in 9 children.

Of these two had fasted for 12 hours, four for 13 hours and three had fasted for 15 hours.

A large proportion of patients (354 out of 475) had plasma glucose between 70mg/dl to 99 mg/dl.

Suprisingly, 71 patients had a fasting plasma glucose level above 100 mg/dl.

There is evidence to suggest that impaired fasting glucose in childhood predisposes to type 2 diabetes mellitus in adulthood . Therefore, hypothetically these tests can be used as part of a screening tool to assess adulthood risk of developing type 2 Diabetes mellitus.

FASTING PLASMA GLUCOSE DISTRIBUTION:

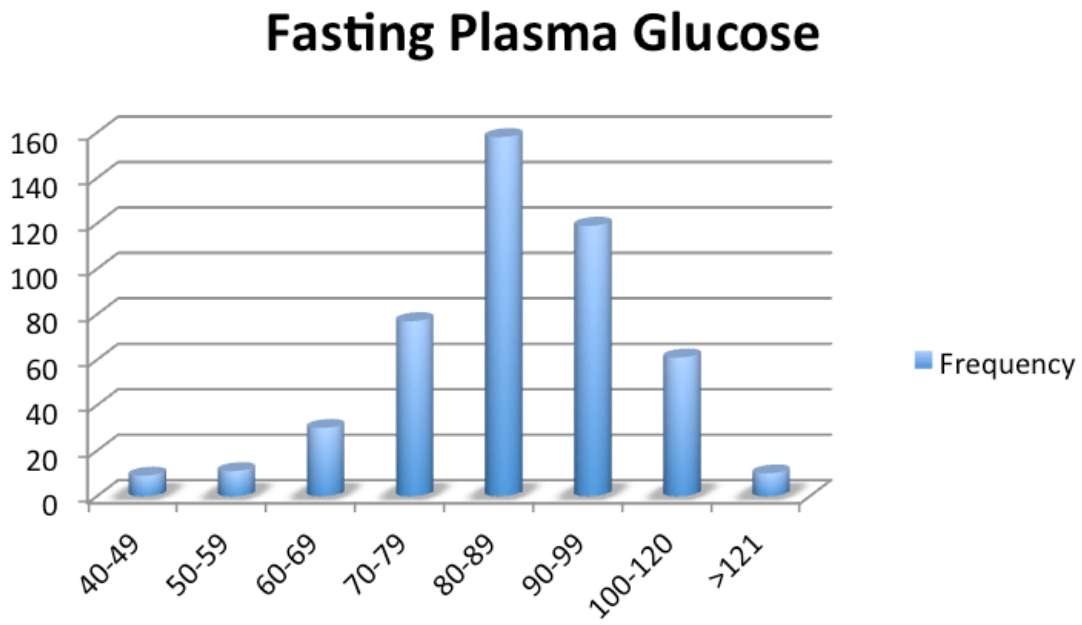


FIGURE 5:

Above is a graphical representation of fasting plasma glucose distribution.

The above graph shows that the majority (354 out of 475) had glucose values between 70 – 100 .

TABLE 6 : PRE OPERATIVE FASTING WITH BLOOD SUGAR LEVELS WITH DURATION OF FASTING (LIQUIDS)

FASTING FOR LIQUIDS (HOURS)	BLOOD SUGAR								TOTAL
	40-49	50-59	60-69	70-79	80-89	90-99	100-120	>121	
2	0	0	0	2	4	2	0	0	8
3	0	2	0	5	5	5	1	0	18
4	0	1	2	8	34	13	7	3	68
5	0	2	3	12	11	22	3	2	55
6	0	2	2	6	13	18	1	0	42
7	0	0	10	6	11	4	6	2	39
8	0	0	2	6	18	5	8	0	39
9	0	0	3	4	5	14	7	2	35
10	0	4	0	6	15	5	11	0	41
11	0	0	0	8	9	10	5	0	32
12	2	0	0	6	10	12	8	0	38
13	4	0	3	0	9	0	3	1	20
14	0	0	3	7	4	4	1	0	19
15	3	0	2	0	4	0	0	0	9
16	0	0	0	0	0	5	0	0	5
18	0	0	0	0	2	0	0	0	2
19	0	0	0	1	0	0	0	0	1
Total	9	11	30	77	154	119	61	10	471

A total of 94 children (20% of the study population) had fasted for longer than 12 hours. There was no correlation between the duration of fasting and the plasma glucose levels measured at induction.

TABLE 7 : PRE OPERATIVE FASTING WITH BLOOD SUGAR LEVELS WITH DURATION OF FASTING (SOLIDS) :

	BLOOD SUGARS								
	40-49	50-59	60-69	70-79	80-89	90-99	100-120	>121	Total
6	0	0	0	4	9	2	2	0	17
7	0	0	0	2	3	0	1	0	6
8	0	0	0	2	7	6	4	0	19
9	0	0	0	5	4	14	5	2	30
10	0	0	0	6	15	5	13	1	40
11	0	2	2	11	5	7	4	0	31
12	2	0	0	8	21	17	12	0	60
13	2	0	0	0	9	8	3	3	25
14	0	2	3	10	5	3	3	2	28
15	3	0	2	1	6	1	1	0	14
16	0	0	3	2	4	8	2	0	19
17	0	0	5	2	1	2	0	0	10
18	0	0	3	0	2	0	3	0	8
19	0	0	0	1	0	0	0	0	1
20	0	0	0	0	1	0	0	0	1
30	0	0	0	2	0	0	0	0	2
36	0	0	0	1	0	1	0	0	2
48	0	0	0	3	0	0	0	0	3
Total	7	4	18	60	92	74	53	8	316

A large proportion of patients (17 children) had fasted for solids for durations greater than 18 hours with three of them having fasted for as much as three days. These were patients who were scheduled to undergo surgical procedures of the bowel requiring long duration bowel preparation. The other reason for such prolonged duration of fasting for solids can again be attributed to the fact that clinicians are especially reluctant to order for light meals approximately six hours prior to the procedure as per the guidelines to allow for other factors like, unforeseen cancellation of previous cases and delayed gastric emptying which may be seen in patients awaiting procedures.

Bivariate correlation was done between various sets of variables and the Pearson's correlation coefficient obtained was interpreted to identify positive linear, low positive, negative or no correlation. A Pearson's coefficient close to +1 is said to have high positive correlation between the variables. A Pearson's coefficient close to -1 is said to have strong negative correlation between the variables. Other values of the coefficient can be interpreted as a gradient between +1 to 0 to -1. All values of the Pearson's coefficient should be accompanied with a statistically significant p value.

A **scatter plot** to graphically visualize the correlation between two variables can be done where the slope of the graph is $(r)^2$, where "r" is the Pearson's correlation coefficient.

In a scenario if variables are said to have a high positive correlation, then **linear regression** between them can be calculated to arrive at a regression equation which helps to determine the dependent variable from the independent variable as below:

Independent variable = 'B constant' + factor x dependent variable.

CORRELATION ANALYSIS BETWEEN FASTING FOR LIQUIDS AND BLOOD SUGAR LEVELS

Pearson's correlation coefficient: -0.47

p value: 0.30

This shows no correlation between the two variables as shown in the scatter plot below.

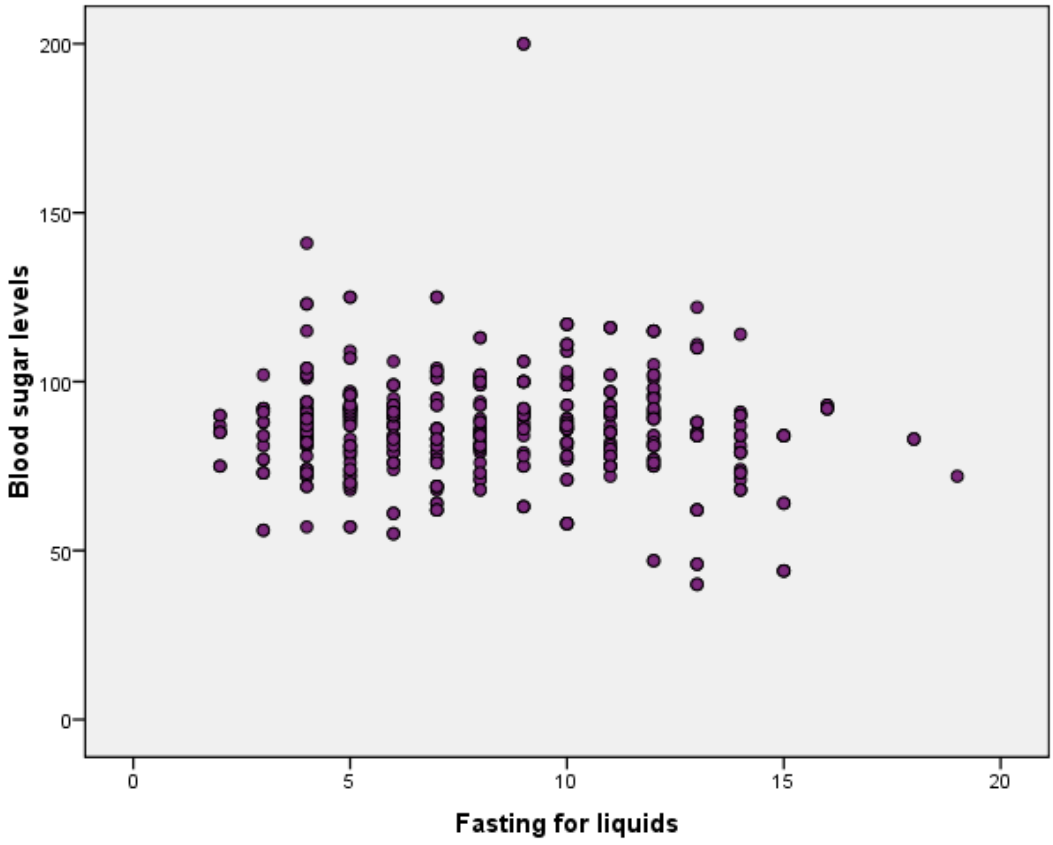


FIGURE 6:

CORRELATION ANALYSIS BETWEEN FASTING FOR SOLIDS AND BLOOD SUGAR LEVELS

Pearson's correlation coefficient: -0.14

p value: 0.10

This shows no correlation between the two variables as shown in the scatter plot below.

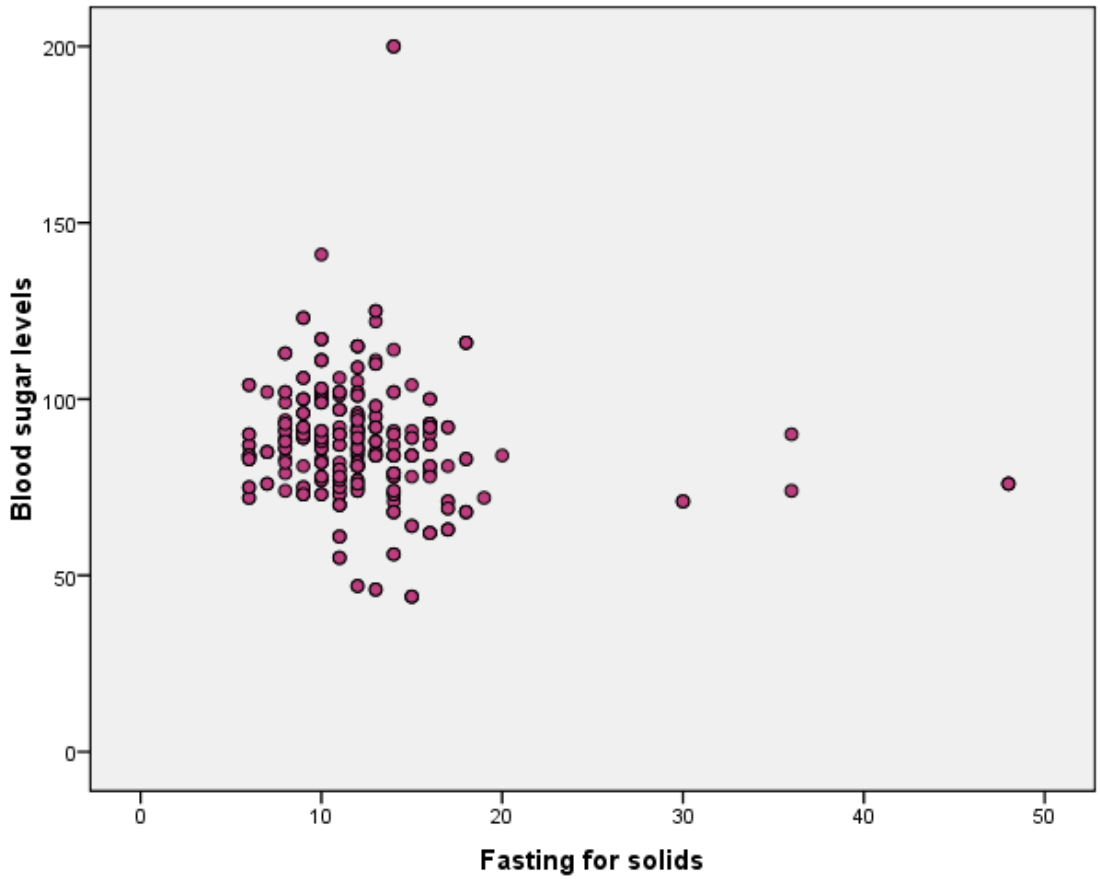


FIGURE 7:

CORRELATION ANALYSIS BETWEEN DURATION OF SURGERY AND DURATION OF EYE OPENING

Pearson's correlation coefficient: 0.08

p value: 0.08

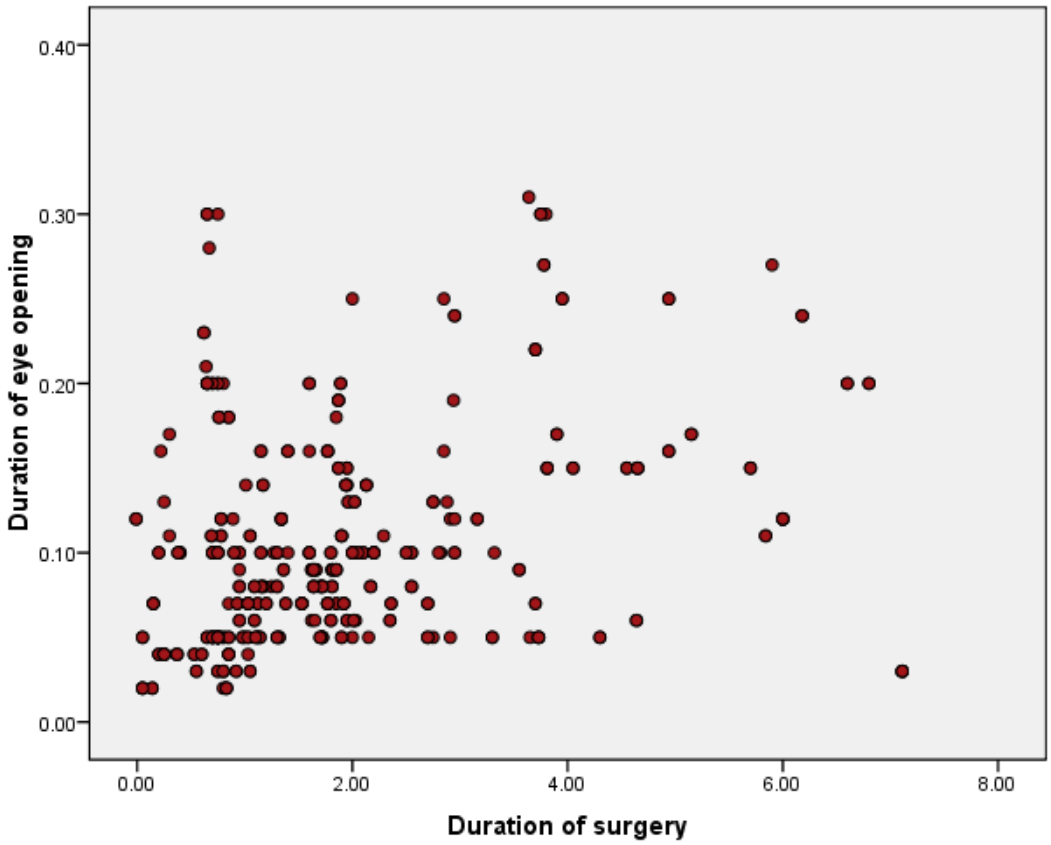


FIGURE 8:

On performing a regression analysis looking for correlation between duration of surgery with duration to eye opening it was noted that there was no correlation between the two variables as shown in the scatter plot above. During the course of the study it was noted that eye opening frequently happened in the recovery room and not in the operation theatre. The time at eye opening on the ensuing data sheets were not entirely accurate. This could be a contributing factor to the results that were subsequently obtained.

7. DISCUSSION :

Preoperative fasting is the practice that requires a patient to be nil per oral (abstaining from oral food and fluid intake) for a pre determined period prior to a surgical procedure . This practice was introduced in the middle of the 19th century to minimize vomiting associated with the agent prevalent at that time namely chloroform. This practice came into widespread use as clinicians the realization dawned that fasting also prevented regurgitation of stomach contents which in turn prevented pulmonary aspiration during general anesthesia.

Till around the time of the second world war pre operative fasting was in widespread use with textbook fasting guidelines of 2–3 hours for clear liquids and 4–6 hours for easily digestible solids. It was around this time that Mendelsson described his “asthma like syndrome” which was associated with pulmonary aspiration and carried with it a very high mortality rate. Subsequently, due to the paranoia surrounding pulmonary aspiration “NPO after 12 midnight” fasting orders came into vogue.

During the course of the next three to four decades evidence began to gradually emerge that this prolonged

fasting was unwarranted and that this enforced long duration fasting carried with it its own side effects described in detail a little later. A culmination of all the new evidence led to the promulgation of the American society of Anaesthesiologists fasting guidelines towards the end of the previous century.

Despite this, prolonged fasting is often an inevitable byproduct of overzealous fasting orders , uncertainties in case schedules, unforeseen cancellation of cases and other vagaries associated the running of an operation theatre list . In addition to the above there is the ever present danger of pulmonary aspiration in children who have inadequate periods of fasting or those with prolonged gastic emptying times.

The above issues often result in children fasting for durations much longer than required as natural instinct forces clinicians to err on the side of “adequate fasting” rather than be faced with a patient presenting to the operating room with “borderline” or inadequate fasting.

This prolonged fasting in not without its own set of problems. Recent research suggests that prolonged fasting is associated with unwanted effects such as thirst, hunger, anxiety, drowsiness, and dizziness. In addition excessive preoperative fasting may have adverse physiologic effect such as dehydration, insulin resistance, postoperative hyperglycemia, muscle

wasting, and a weakened immune response.

Since side effects like thirst and hunger are more easily ignored by the clinician and the physiological side effects are often clinically intangible when compared to the complications that spring to mind when faced with the prospect of a patient with pulmonary aspiration it is therefore very tempting for the treating physicians to tailor the fasting order with the sole objective of preventing the dreaded complication of pulmonary aspiration . Therefore a common occurrence in hospitals arount the world is children presenting to the operating theatre having fasted longer inordinately long periods.

In addition to the above mentioned complications hypoglycaemia is a frequently mentioned byproduct of prolonged fasting. However the association between preoperative fasting and hypoglycemia has been controversial. Various studies done at different points in time have shown levels of hypoglycaemia ranging from 10% to 30% as well as studies showing no effect on blood glucose levels after prolonged periods of fasting.

Previous studies to assess the association between prolonged fasting and hypoglycaemia that have been done, studied other population groups. Studies on our population group have been few and inconclusive. Hence there was a need to carry out a study with a sufficiently large sample size to establish a causal

relationship between the two if any.

For this study all the usual protocols were followed during the perioperative period in all aspects including the administration of fasting orders. Tinkering with and altering fasting orders could have been deemed unethical and may not been able to withstand the scrutiny of the ethics committee. Hence the study was designed to be an observational study. A total of 475 childen were included in the study with plasma glucose levels being measured for each of them at induction.

The following end points were looked for :

1. Duration of fasting for in children undergoing elective surgical procedures.
2. Clinical features of hypoglycemia at induction.
3. Fasting blood sugar levels at induction.
4. Delayed awakening attributable to hypoglycemia subsequent to prolonged fasting.

With regards to the first end point namely duration of fasting in children undergoing elective surgical procedures it was seen that despite knowledge of the study that was being done , yet a total of 94 children (20% of the study population) had fasted for longer than 12 hours. In addition it was also seen that the duration of fasting for solids was more than 12 hours for almost one in every three patients. Therefore there is a need for more measures to be introduced into the standard operative procedures to reduce the proportion of children who end up fasting for such lengthy durations. At the outset this may seem like an easy change to make but when faced with the pressures of an overburdened theatre list along with obligations to accommodate unpredictable emergency procedures this is certainly not a task to be taken lightly.

With regards to the second end point namely clinical features of hypoglycemia at induction there were 4 children in the study with clinical features of hypoglycemia. However they all had normal blood glucose levels. This can be attributed to the fact that the features of hypoglycaemia like irritability , lethargy among others are not very specific. The questionnaire given to the health care providers prior to the case did not mention specific features of hypoglycaemia to look for. Hence the low number of patients with clinical features of hypoglycaemia could be attributed to this lack of standardization.

With regards to the third end point namely fasting blood sugar levels at induction our study showed that children presented to the operating room with normal blood glucose levels irrespective of the duration of pre operative fasting. This however should not be used as a justification for indiscriminate fasting orders as a lot of other undesirable side effects like thirst, hunger, anxiety, drowsiness, and dizziness are associated with excessive preoperative fasting. Other unwanted physiologic effects, including dehydration, insulin resistance, postoperative hyperglycemia, muscle wasting, and a weakened immune response are also frequently seen. It also needs to be kept in mind that with the sample size of this study only an absolute precision close to 1.5% was achieved. That means a similar study conduction on the same sample size could result in 1.5% of the study subjects having hypoglycemia. Hence low plasma glucose levels at induction are not completely ruled out by this study. To achieve an absolute precision of 0.5% would have required a sample size of approximately 5000 children which was beyond the scope of this study. Hence the fact that none of the children in this study developed hypoglycemia cannot be used as justification for indiscriminate use of the “npo after 12 midnight “ fasting order.

With regards to the fourth end point namely delayed awakening attributable to hypoglycemia at induction subsequent to prolonged fasting since there were no children with low sugar levels at induction we can safely assume that prolonged awakening need not be attributed to hypoglycemia at induction. However it was observed during the study that a large proportion of patients approximately 10%) had experienced some form of delayed awakening. Since this study looked at only one of the myriad causes of delayed awakening we were not able to attribute causes for each of the cases of delayed awakening. This could form the focus of investigative questions of a future study.

8. LIMITATIONS :

1. This study has been done only on otherwise healthy children coming for elective procedures . Hence these results may not apply to children with acute as well as chronic disease conditions and those coming for emergency procedures.
2. The adverse effects of prolonged fasting many but this study addresses only one of them namely its effects on blood glucose levels. There are many more facets and side effects to long duration fasting in children . Therefore these results can by no means be used to justify excessive starvation periods prior to procedures.
3. The sample size for this study was 475 children works out to an absolute precision of approximately 1.5% - meaning the study does not rule out absolutely the possibility of hypoglycaemia due to prolonged fasting in this cohort. A sample size of 5333 would have required to achieve an absolute precision of 0.5% - this would not have been possible to achieve given the time limitations associated with this study.
3. Ways and methods to reduce the duration of un necessary fasting need to be actively explored in future studies as the fraction of children who end up fasting for long durations seems to be significant.

4. The study also attempted to delineate delayed awakening attributable to hypoglycaemia at induction. Though there were patients who experienced delayed awakening during the course of the study the reasons behind the same could not be pin pointed as the study looked for just a single cause. Since all the patients had normal blood sugar levels none of the cases of delayed awakening could be attributed to the same.

With all the above limitations in mind it can still be concluded that the study was able to accomplish most of objectives that were envisioned at the onset.

9. CONCLUSIONS :

In this study evaluating the effects of pre operative fasting in children under the age of 60 months on blood sugar levels at induction as well as its role in delayed awakening we reached the following conclusions :

1. Fasting in children though detrimental in more ways than one did not cause hypoglycemia even when fasting longer than expected. Routine measurement of blood glucose levels in otherwise healthy children is therefore not warranted.
2. As none of the children who fasted for longer than 12 hours developed hypoglycemia we can safely assume that there is no link between pre operative fasting and duration to awakening attributable to pre op glucose levels.
3. Delayed awakening in children without a co existing metabolic disorder is unlikely to be due to hypoglycemia.
4. Almost one in five children had fasted for longer than 12 hours and though the duration did not affect fasting blood sugar levels, other side effects were observed in the children.

To summarize, **prolonged fasting does not lead to hypoglycemia prior to induction nor does it lead to delayed awakening secondary to hypoglycemia in otherwise healthy children below the age of 60 months**.

10. BIBLIOGRAPHY :

1. Oxford Handbook of Anaesthesia,
   (Keith G. Allman n.d., 1) 2nd edition Oxford University Press 2006

2. Textbook of Anaesthesia, Smith (1997)

3. Green et al (1996) and Jester and Williams (1999)

4. Preoperative fasting guidelines, Maltby JR, Can Journal of Surgery, volume 49, issue 2 ,pages=138–9 ,April 2006

5. Preoperative preparation and premedication, Coté CJ,
   Br J Anaesth ,volume 83 issue 1 pages=16–28,
   July 1999.

6. Maltby JR. Fasting from midnight- the history behind the dogma. *Best Pract Res Clin Anaesthesiol* 2006;20(3):363-78.

7. Lister J. On anaesthetics. In: Holmes system of surgery. 3rd ed. London: Longmans Green and Co.; 1883

8. Stuart PC. The evidence base behind modern fasting guidelines. *Best Pract Res Clin Anaesthesiol* 2006;20(3):457-69.

9. Pandit UA, Pandit SK. Fasting before and after ambulatory surgery. *J Perianesth Nurs* 1997;12(3):181-7.
10. Soreide E, Ljungqvist O. Modern preoperative fasting guidelines: a summary of the present recommendations and remaining questions. *Best Pract Res Clin Anaesthesiol* 2006;20(3):483-91.
11. Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anesthesia. *Am J Obstet Gynecol*1946;52:191-205.
12. Preoperative fasting for adults to prevent perioperative complications. Can J Surg 2005;48 :409-11.
13. McLeod R, Fitzgerald W, Sarr M; for Members of the Evidence Based Reviews Surgery Group. Canadian Association of General Surgeons and American College of Surgeons evidence based reviews in surgery.
14. Maltby JR, Sutherland AD, Sale GP, et al. Preoperative oral fluids: Is a five hour fast justified prior to elective surgery? Anesth Analg 1986;65: 1112-6.
15. American Society of Anesthesiologists Task Force on Preoperative Fasting. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: a report by the

American Society of Anesthesiologists Task Force on Preoperative Fasting. Anesthesiology 1999; 90:896-905.

16. Canadian Anesthesiologists' Society. Guidelines to the practice of anesthesia. Toronto: the Society; 2000.

17. Payne K, Ireland P. Plasma glucose levels in the perioperative period in children. Anaesthesia 1984; 39: 868-72.

18. American society of Anesthesiologists Task Force on Preoperative Fasting. Practice guidelines for preoperative fasting and the use of pharmacological agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. Anesthesiology 1999; 90: 896-905.

19. Watson BG. Blood glucose levels in children during surgery. Br J Anaesth 1972; 44: 712-15.

20. Bevan JC, Burn MC. Acid-base changes and anaesthesia. Anaesthesia 1973; 28: 415.

21. Graham IFM. Preoperative starvation and plasma glucose concentrations in children undergoing outpatient anaesthesia. Br J Anaesth 1979; 51: 161-64.
22. Jensen BH, Wernberg M, Andersen M. Preoperative starvation and blood glucose concentrations

children undergoing inpatient and outpatient anaesthesia. Br J Anaesth 1982; 54: 1071-74.

23. Thomas DKM. Hypoglycemia in children before operation: Its incidence and prevention. Br J Anaesth 1974; 46:66-68.

24. Bowie MD, Mulligan PB, Schwartz R. Intravenous glucose tolerance in the normal newborn infant: the effects of a double dose of glucose and insulin. Pediatrics 1963; 31:590.

25. Bevan JC, Burn MC. Acid-base and blood glucose levels of paediatric cases at induction of anaesthesia: the effects of preoperative starvation and feeding. Br J Anaesth 1973; 45: 115.

26. Prolonged fasting in pediatric outpatients does not cause hypoglycemia**.** Huang SJ, Lee KC, Lai YY, Su HP, Tsai YC, Yeh FC, Chang CL. Department of Anesthesiology, National Cheng Kung University, Medical College and Hospital, Tainan, Taiwan, R.O.C J Med Assoc Thai. 1996 Apr;79(4):236-9.

27. Preoperative Fasting and Plasma Glucose Levels in Children
Pramod Gupta, R. Sehgal, H.M. Krishna J Anaesth Clin Pharmacol 2004; 20(2)

28. American Society of Anesthesiologists Committee on Standards and Practice Parameters. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology* 2011;114(3):495-511.

29. American Society of Anesthesiologists Task Force on Preoperative Fasting. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: a report by the American Society of Anesthesiologist Task Force on Preoperative Fasting.*Anesthesiology* 1999;90(3):896-905.

30. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 2002;96(4):1004-17.

31. Agarwal A, et al. Fluid deprivation before operation. The effect of a small drink. *Anaesthesia* 1989;44(8):632-4.

32. Maltby JR, et al. Gastric fluid volume, pH, and emptying in elective inpatients. Influences of narcotic-atropine premedication, oral fluid, and ranitidine. *Can J Anaesth* 1988;35(6):562-6.

33. Sutherland AD, et al. The effect of preoperative oral fluid and ranitidine on gastric fluid volume and pH. *Can J Anaesth*1987;34(2):117-21.

34. Melis GC, et al. A carbohydrate-rich beverage prior to surgery prevents surgery-induced immunodepression: a randomized, controlled, clinical trial. *JPEN J Parenter Enteral Nutr* 2006;30(1):21-6.

35. Nygren J. The metabolic effects of fasting and surgery. *Best Pract Res Clin Anaesthesiol* 2006;20(3):429-38.

36. Nygren J, et al. Are there any benefits from minimizing fasting and optimization of nutrition and fluid management for patients undergoing day surgery? *Curr Opin Anaesthesiol* 2007;20(6):540-4.

37. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg*2008;248(2):189-98.

38. Ljungqvist O. Modulating postoperative insulin resistance by preoperative carbohydrate loading. *Best Pract Res Clin Anaesthesiol* 2009;23(4):401-9.

39. Hausel J, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. *Anesth Analg*2001;93(5):1344-50.

40. Yuill KA, et al. The administration of an oral carbohydrate-containing fluid prior to major elective

upper-gastrointestinal surgery preserves skeletal muscle mass postoperatively-a randomised clinical trial. *Clin Nutr* 2005;24(1):32-7.

41. Ljungqvist O, et al. Modulation of post-operative insulin resistance by pre-operative carbohydrate loading. *Proc Nutr Soc*2002;61(3):329-36.

42. Ljungqvist O, et al. Preoperative nutrition-elective surgery in the fed or the overnight fasted state. *Clin Nutr*2001;20(Suppl 1):167-71.

43. Soop M, et al. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. *Am J Physiol Endocrinol Metab* 2001;280(4):E576-E583.

44. Svanfeldt M, et al. Effect of "preoperative" oral carbohydrate treatment on insulin action-a randomised cross-over unblinded study in healthy subjects. *Clin Nutr* 2005;24(5):815-21.

45. Svanfeldt M, et al. Randomized clinical trial of the effect of preoperative oral carbohydrate treatment on postoperative whole-body protein and glucose kinetics. *Br J Surg* 2007;94(11):1342-50.

46. Hausel J, et al. Randomized clinical trial of the effects of oral preoperative carbohydrates on postoperative nausea and vomiting after laparoscopic cholecystectomy. *Br J Surg* 2005;92(4):415-21.

47. Noblett SE, et al. Pre-operative oral carbohydrate loading in colorectal surgery: a randomized controlled trial. *Colorectal Dis* 2006;8(7):563-9.

48. Delayed Awakening Or Emergence From Anaesthesia Vellore, India © *World Federation of Societies of Anaesthesiologists.*

11. APPENDIX

11.1 Data sheet

11.2 Intructions to anaesthetists

11.3 Information sheet

11.4 Informed consent

11.1 PAEDIATRIC HYPOGLYCAEMIA DATA SHEET

Date:

S.No

a. Name

b. Age

c. Sex – M / F

d. Hospital Number

e. Diagnosis

Preoperative

1. Time of last intake of food:
    - Liquids
    - Solids
2. Weight:
3. Symptoms of hypoglycaemia:
4. Blood glucose level:
5. Time at induction:

Investigations :

1. Hemoglobin
2. Creatinine

Induction :

Collect sample for glucose levels when the iv access is obtained.

Fentanyl given at induction ☐

Enter hemodynamic parameters (Bp/HR) for 1st one hour only.

For MAC column – Record isoflurane setting.

For Drugs to attenuate response record all drugs given to alter BP/HR

Intraoperative – ALL TIMES/VALUES TO BE RECORDED FROM THE MONITOR

- Please record the following in yellow-sheet:

1. **Hemodynamic values every 5 minutes**

TIME									
BP									
HR									
MAC									
DRUGS TO ATTENUATE RESPONSE									
TIME									
BP									
HR									
MAC									
DRUGS TO ATTENUATE RESPONSE									
TIME									
BP									
HR									
MAC									
DRUGS TO ATTENUATE RESPONSE									

- TIME AT INTUBATION/LMA PLACEMENT:
- TIME AT SKIN INCISION:
- TIME WHEN INHALATIONAL AGENT IS STOPPED:
- TIME AT EYE OPENING:

  (Time at which patient opens the eyes, either spontaneously or on verbal prompting repeated every 2 min)

PAIN MODALITIES -

- **Total Additional Fentanyl consumption:** ☐
- **Caudal/ epidural drug dosage :** ☐

11.2 INTRUCTIONS TO ANAESTHETISTS

All children under the age of 5 are eligible to be included unless specified.

Fasting orders to be written as usual
At the control desk
Get consent from the parents if not taken already.

Please remember to take back the information sheet and signed consent forms back from the parents

Note exact age of the child in months and exact time of last intake of liquids and solids

After induction and placement of IV line collect 2 ml of blood in the grey tube provided.
ASAP send the sample to the lab after labelling the tube and the biochemistry slip with the bradma.
Fill in the data sheet with the relevant information during the case.
At the end of the case please leave the data sheet and other material in the CB 1 DD cupboard.

11.3 INFORMATION SHEET :

Christian Medical College, Vellore
Department of Anaesthesiology

Fasting and Plasma Glucose Levels in Children

Information sheet

You are being requested to participate in a study to see the effect of preoperative fasting. We hope to include about 400 children from this hospital in this study.

Why are patients required to fast prior to surgery?

Patients posted for elective surgeries are required to fast prior to surgery, mainly to prevent aspiration which is the regurgitation of stomach contents into the lungs. Uncertainties in case schedules, unforeseen cancellation of cases and failure to comply with preoperative fasting instructions often lead to preoperative fasting longer than what is required.

Does taking part involve any additional risk?

There will be no modification of the treatment protocols if you take part in the study. That is the treatment you receive at the hospital will be the same regardless of whether you take part in the study or not.

If you take part what will you have to do?

If you agree to participate in this study, there will be no modification to your pre operative preparation that is you will undergo pre operative investigations, receive medications and fast for the surgery as deemed necessary by the doctors treating you. The fact that you are taking part in the study will have no bearing on the above. Prior to surgery the usual protocol is to start an intravenous line for the child just after or if co operative just prior to inducing anaesthesia. This (starting of an intravenous line) is done for all cases. The only change will be the 2 ml of blood that will be collected from your child when the intravenous line is started for the case. We will also be using some blood pressure and heart rate recordings from the anaesthesia record during the procedure.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the study tests?

NO. The money for the extra test will come from a research fund and you will not need to pay for the same.

Any other treatment that you usually take will continue but the usual arrangements that you have with the hospital will decide how much you pay for this.

What happens after the study is over?

Your child will undergo management as is routinely done for paediatric cases everyday, with patient safety being the primary concern. There will be no modification of the same as a result of the study during or after the study.

Will your personal details be kept confidential?

The results of this study may published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

11.4 INFORMED CONSENT :

Study Title: Fasting and Plasma Glucose Levels in Children

Study Number:

Participant's name:

Date of Birth / Age (in years):

I_____

_____

_____, father/mother of

_____

Declare that I have read the information sheet provide to me regarding this study and have clarified any doubts that I had.

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights

I also understand that neither I, nor my doctors, will alter the treatment protocols as a result of my child taking part in the study

I understand that the extra tests that this study entails will be done free of cost but I will not receive and other financial compensation

I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access

I understand that my identity will not be revealed in any information released to third parties or published

I voluntarily agree to take part in this study

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date: